

3-D TOMOGRAPHIC RECONSTRUCTION OF THE AVERAGE PROPAGATOR FROM MRI DATA

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ABSTRACT

The measurement of the 3-D “average propagator”, $P(\mathbf{r})$, from diffusion-weighted (DW) NMR or MRI data has been a “holy grail” in materials science and biomedicine, as $P(\mathbf{r})$ provides detailed microstructural information, particularly about restriction, without assuming an underlying diffusion model. While Callaghan proposed a 3-D Fourier transform relationship between $P(\mathbf{r})$ and the DW signal attenuation, $E(\mathbf{q})$ [1], using it to measure $P(\mathbf{r})$ from $E(\mathbf{q})$ data is not currently feasible biologically or clinically, owing to the staggering amount of DW data required.

To address this problem, we propose that computed tomography principles can be applied to reconstruct $P(\mathbf{r})$ from DW signals. Moreover, this reconstruction can be performed efficiently using many fewer DW $E(\mathbf{q})$ data as compared to conventional 3-D q -space MRI [1] or Diffusion Spectrum Imaging (DSI) [2] by employing *a priori* information about $E(\mathbf{q})$ and $P(\mathbf{r})$.

1. INTRODUCTION

Q -space nuclear magnetic resonance (q -NMR) is an experimental and theoretical framework originally developed by Cory [3] and Callaghan [4] to characterize features of the displacement distribution of translating spin-labeled molecules. Specifically, they proposed using a pulsed-gradient NMR experiment to measure the “average propagator”, $P(\mathbf{r})$, of spin-labeled molecules directly from the MR echo using a Fourier transform relationship.

The power and utility of this approach stems from its ability to characterize random and bulk molecular displacements in optically turbid media without having to invoke a specific model of the translational diffusion process or of the material’s microstructure. In fact, these can often be inferred from the MR data itself. For instance, by examining the dependence of the MR signal as a function of the diffusion time, and of the length scale probed (as measured by the \mathbf{q} vector), one can extract useful morphological features, particularly in porous media, such as the pore size and even the size distribution of pores, tubes, and plates.

Three-dimensional q -space Magnetic Resonance Imaging (3-D q -space MRI), again proposed by Callaghan [1, 4], entails combining a q -space NMR experiment within

a conventional MRI. This can be done by performing an NMR q -space experiment followed by an imaging sequence (q -space filtering), or actually embedding an NMR experiment within a conventional MRI sequence. Either way, a 3-D q -space NMR experiment can be performed voxel by voxel within an imaging volume [1, 4]. This imaging modality can provide local information about material microstructure and microdynamics in heterogeneous, anisotropic specimen or samples, which are homogeneous on the length scale of a pixel or voxel.

The potential for 3-D q -space MRI particularly in biological and clinical applications, is enormous but has yet to be realized. Assaf et al. have shown differences in features of the average propagator in neurological disorders, such as multiple sclerosis (MS) [5]. Another possible application is to use information provided by the average propagator to resolve nerve or muscle fiber bundles in regions where such fibers cross. Because of the recently demonstrated strong orientational dependence of the q -space data with fiber angle, there is a suggestion that 3-D q -space imaging could significantly improve the resolution of fiber orientation beyond that provided by diffusion tensor MRI [6, 7].

However, there are a number of significant obstacles that currently preclude the application of 3-D q -space MRI *in vivo*. The first is that it is not feasible to satisfy the “short pulse gradient” approximation in animal and human MRI systems, because the rapidly switched currents required to produce such gradients induce electric fields in the body that would exceed the current FDA threshold for cardiac, CNS and peripheral nerve stimulation. This short pulse condition is required for the 3-D Fourier Transform relationship between the displacement distribution and the MR signal to be strictly valid. To ameliorate this problem, one can use longer duration, smaller amplitude magnetic field gradients. While this precludes measuring the displacement distribution directly, it still allows us to measure the average propagator, which is a smoothed version of this distribution.

The second and more significant obstacle to performing 3-D q -space MRI is the large number of diffusion weighted MRI data points required to reconstruct the average propagator, itself. Using the classical method of 3-D q -space MRI first proposed by Callaghan [1,4] and later recast as Diffusion Spectrum Imaging (DSI) by Wedeen et al. [8], the average propagator is obtained from a 3-D IFFT

of $E(\mathbf{q})$ data that is sampled uniformly over the 3-D q -space. The thousands of DWI data samples required make this approach infeasible for routine animal and clinical imaging. For instance, a recent study of ischemia in rat brain took 56 hours to acquire sufficient q -space data to be able to reconstruct the average propagator. DSI studies in humans have been reported to take 6 hours.

To address this burden of long MR scans, several methods have been proposed to reconstruct particular features of the average propagator while using a reduced number of acquisitions. For example, Q-Ball MRI [9] was introduced to provide an estimate of the radially averaged propagator or orientational distribution function (ODF). Other analysis methods have been proposed to try to reconstruct features of the ODF, including PAS-MRI [10,11], Generalized Diffusion Tensor MRI (GDTI) [12,13]. All of these methods entail acquiring a high angular resolution diffusion imaging (HARDI) data set, using a smaller number (e.g., 256) of DWI acquisitions sampled on a spherical shell in q -space.

While providing useful information about the orientation bias of diffusion in tissue and possibly other anisotropic media, the ODF itself contains only a small part of the total information content provided by the average propagator. For instance, from the ODF, one cannot recover the Gaussian part of the average propagator that provides the same information provided by diffusion tensor MRI (DTI) [14], or the statistical features of the average propagator, including high-order moments.

Our goal here is to estimate the entire average propagator from MR diffusion weighted data but using a vastly reduced number of DWIs than is presently required. This economy is achieved by introducing two new ideas. One is recasting the estimation of the average propagator from the MR signal as a problem in computed tomography (CT). The second is the incorporation of *a priori* information in the reconstruction of the average propagator from DWI data rather than using the brute force 3-D FFT proposed in [8] for which no *a priori* information about the MR experiment or the properties of the functions themselves. Using these ideas together, we are able to achieve acceptable reconstructions of the average propagator in a clinically feasible time period.

Specifically, we show how to recast the estimation of $P(\mathbf{r})$ from $E(\mathbf{q})$ in each voxel as a tomographic reconstruction problem. First, we provide a probabilistic interpretation of 1-D q -space data, $E(\mathbf{q})$, as the Fourier transform of the marginal distribution of $P(\mathbf{r})$ obtained along the same direction in displacement space. This analogy suggests an alternative sampling scheme of 3-D q -space MR data by acquiring several 1-D acquisitions of $E(\mathbf{q})$ data along different rays in q -space. Then, by applying *a priori* information about the properties of $P(\mathbf{r})$ and $E(\mathbf{q})$, we are able to constrain the reconstruction of $P(\mathbf{r})$, allowing us to use a limited number of “views” or projections of $P(\mathbf{r})$ than currently required. In this case, the inversion of $P(\mathbf{r})$

from $E(\mathbf{q})$ data is performed iteratively with a scheme used in other tomographic reconstruction applications [15,16].

2. THEORY

Here we offer an alternative probabilistic interpretation of $E(\mathbf{q})$ obtained along a particular ray in q -space. It is the 1-D Fourier transform of the marginal density of $P(\mathbf{r})$ along a ray in real space that is parallel to \mathbf{q} . To see this, consider the following:

Suppose we have a function $P(x,y,z)$ and we are interested in computing its marginal distribution along a particular direction. For this example, assume that the direction is $\mathbf{n}=(x,0,0)$, $p_x(x) = \iint P(x,y,z) dy dz$, for simplicity,

however, the same analysis can be done for a general \mathbf{n} , since one can always rotate the sample so that the desired \mathbf{n} is aligned with the direction above. If the signal measured in q -space imaging is the Fourier transform of $P(x,y,z)$, then we have:

$$E(q_x, q_y, q_z) = \iiint P(x,y,z) e^{-i2\pi(q_x x + q_y y + q_z z)} dx dy dz, \quad (1)$$

where \mathbf{q} specifies the strength and direction of the diffusion-sensitizing gradient and $E(q_x, q_y, q_z)$ is the complex measured signal. Setting $q_y = q_z = 0$, we have:

$$\begin{aligned} E(q_x, 0, 0) &= \iiint P(x,y,z) e^{-i2\pi q_x x} dx dy dz \\ &= \int \left(\iint P(x,y,z) dy dz \right) e^{-i2\pi q_x x} dx \end{aligned} \quad (2)$$

Substituting the expression for $p_x(x)$ into (2), we have

$$E(q_x, 0, 0) = E(q_x) = \int p_x(x) e^{-i2\pi q_x x} dx. \quad (3)$$

But (3) is just the 1-D Fourier transform of $p_x(x)$, which means that $p_x(x)$ can be computed by a 1-D inverse Fourier transform:

$$p_x(x) = \int E(q_x) e^{i2\pi q_x x} dq_x. \quad (4)$$

This means that if one wants to compute the profile of the function $P(x,y,z)$ along a particular direction $\mathbf{n}=(x,0,0)$, all that is needed is the $E(q_x, 0, 0)$ data, from which the profile $p_x(x)$ can be computed from equation (4). Suppose we were to acquire $E(\mathbf{q})$ data along different rays in q -space. The FFT of these data would represent marginal distributions of $P(\mathbf{r})$ obtained along different orientations in displacement space. A question that arises is whether it is possible to obtain an accurate estimate of $P(\mathbf{r})$ from a set of marginal distributions of $P(\mathbf{r})$ obtained along different orientations or projections?

A key idea proposed here is to recognize that the determination of $P(\mathbf{r})$ can be viewed as a tomographic

reconstruction of $P(\mathbf{r})$ from several 1-D projections of it obtained along different non-collinear directions. The conventional approach to calculate $P(\mathbf{r})$ by performing a 3-D FFT of uniformly sampled $E(\mathbf{q})$ data does not naturally allow one to incorporate additional *a priori* information that could improve the accuracy of the estimate of $P(\mathbf{r})$ and constrain the solution. For example, we know that

- $P(\mathbf{r})$ is everywhere non-negative,
- $P(\mathbf{r})$ is a scalar,
- $P(\mathbf{r})$ has to sum to 1 throughout the volume,
- $E(\mathbf{q})$ has a quadratic dependence on \mathbf{q} for small \mathbf{q} .

3. ALGORITHM

As shown in Fig. 1, $E(\mathbf{q})$, measured along a ray in q -space, q , is the 1-D Fourier transform of the marginal probability density of $P(\mathbf{r})$, $p_m(r)$, along the corresponding ray in displacement space, r . Tomographic reconstruction can now be applied to the 3-D Radon transform, i.e., to estimate $P(\mathbf{r})$ from different projections, $p_m(r)$. We propose using the iterative procedure of Gerchberg and Papoulis (G-P), originally developed for the 2-D [15] and 3-D ray transforms [16]. While iterating between q - and r -space, all available *a priori* information about the properties of $E(\mathbf{q})$, $P(\mathbf{r})$, and $p_m(r)$ can be applied.

To test our modified G-P algorithm, numerical simulations were performed. In Fig. 2a, the exact $P(\mathbf{r})$ is shown as an isosurface. In Fig. 2b, only 13x13 polar and azimuthal angles, and 9 radial points (1,521 total) along each q vector were sufficient to reconstruct $P(\mathbf{r})$ faithfully. (Assuming a repetition time of 3 seconds, MR acquisition time would be approximately 1.25 hours.) Two constraints were applied during the iterative procedure: positiveness of $P(\mathbf{r})$, and smoothness of $E(\mathbf{q})$ (i.e., Tikhonov regularization). Only four iterations were required to reconstruct $P(\mathbf{r})$ with RMS error =22%. Next, in Fig.3a, we reconstructed $P(\mathbf{r})$ from one voxel of experimental DWI data (excised spinal cord) having 31 directions, each with 16 radial points in q -space [17]. Acquisition time for this data was 34 minutes. Fig.3b shows the restoration of the full real part of $E(\mathbf{q})$.

4. DISCUSSION AND CONCLUSION

In considering the novelty of this new approach, it is important to distinguish it from "tensor tomography" [18] which the diffusion tensor field is reconstructed from DWI data by integrating DWI signal intensities along rays within the imaging volume. Our tomographic reconstruction of $P(\mathbf{r})$ is performed using $E(\mathbf{q})$ data obtained within *each voxel*. Our approach also differs from Q-ball MRI [9,19], which only attempts to reconstruct orientational features of $P(\mathbf{r})$ using $E(\mathbf{q})$ data acquired on a sphere in q space. We use $E(\mathbf{q})$ data obtained throughout q -space to reconstruct the entire propagator, $P(\mathbf{r})$.

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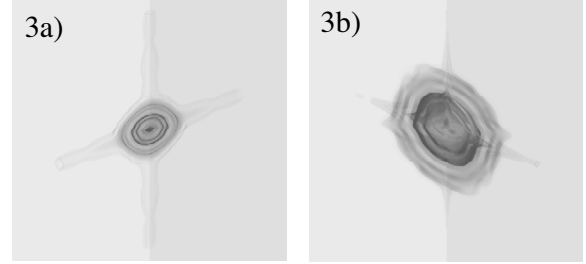


Fig.3. Reconstruction of a) $P(r)$ and b) $E(q)$ from experimental MRI data using a pig spinal cord phantom.

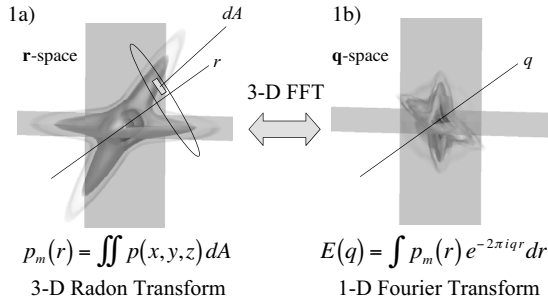


Fig.1. Correspondence between r -space and q -space.

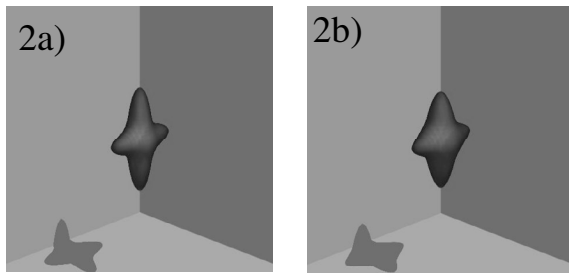


Fig.2. Exact phantom (a) and its reconstruction (b).